

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference E-2549/04	FOR FURTHER ACTION	See item 4 below
International application No. PCT/EP2004/053726	International filing date (<i>day/month/year</i>) 29 December 2004 (29.12.2004)	Priority date (<i>day/month/year</i>) 30 December 2003 (30.12.2003)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant BENATTI, Umberto		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- | | | |
|-------------------------------------|--------------|---|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the report |
| <input checked="" type="checkbox"/> | Box No. II | Priority |
| <input type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> | Box No. VI | Certain documents cited |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input checked="" type="checkbox"/> | Box No. VIII | Certain observations on the international application |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	<table border="1" style="width: 100%; border-collapse: collapse;"> <tr> <td style="padding: 2px;">Date of issuance of this report 03 July 2006 (03.07.2006)</td> </tr> <tr> <td style="padding: 2px;"> Authorized officer <div style="text-align: center; font-weight: bold; font-size: 1.2em;">Ellen Moyse</div> </td> </tr> </table> e-mail: pt05@wipo.int	Date of issuance of this report 03 July 2006 (03.07.2006)	Authorized officer <div style="text-align: center; font-weight: bold; font-size: 1.2em;">Ellen Moyse</div>
Date of issuance of this report 03 July 2006 (03.07.2006)			
Authorized officer <div style="text-align: center; font-weight: bold; font-size: 1.2em;">Ellen Moyse</div>			

PATENT COOPERATION TREATY

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From the
INTERNATIONAL SEARCHING AUTHORITY

P105

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2004/053726

International filing date (day/month/year)
29.12.2004

Priority date (day/month/year)
30.12.2003

International Patent Classification (IPC) or both national classification and IPC
C07K5/02, A61K38/06

Applicant
BENATTI, Umberto

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/053726

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

Box No. II Priority

1. ☒ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43*bis*.1 and 64.1) is the claimed priority date.
2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2004/053726

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-14
	No: Claims	
Inventive step (IS)	Yes: Claims	1-14
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-14
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Section V

1 Reference is made to the following documents:

D1: US-A-5 464 825 (ANDERSON ET AL) 7 November 1995;
D2: WO 98/09986 A (THE MANCHESTER METROPOLITAN UNIVERSITY;
D'SILVA, CLAUDIUS) 12 March 1998.

- 1.1 Document D1 discloses the preparation and use of N-acyl glutathione and glutathione monoalkyl esters "to provide increased intracellular levels of glutathione" (GSH), that is, for the same purpose of the present application (cf. page 3).
- 1.2 Nevertheless, the applicant has demonstrated with comparative tests that N-butanoyl GSH provides a very high antiviral efficacy, associated with a low (or no) cellular toxicity (cf page 11). Therefore, the selection of a specific group of compounds among all possible N-acyl GSH derivatives is regarded as inventive, as the peptides claimed present an unexpected effect in relation to those described in the state of the art.
- 1.3 This authority also acknowledges that there is *prima facie* the reasonable expectation for substantially all compounds of formula (I) being efficacious as antiviral agents, as thiol-protected derivatives are GSH agonists known in the prior art (cf. for example D2).
- 2 In view of the above, the present application satisfies the criteria set forth in Articles 33(2) and 33(3) PCT, because the subject matter of claims 1-14 is new and involves an inventive step in respect of the prior art as defined in the regulations (Rule 64(1)(3) and 65(1)(2) PCT).

Section VIII

The lack of an -OH in the carboxylic group of Gly in formula (I) (cf. page 1 and claim 1) was considered as an obvious error as it is evident from the description and from the MS spectra of Figure 1 that the subject-matter for which protection is sought are N- α -butanoyl (γ -glutamylcysteinylglycine) and its Cys-protected derivatives.